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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,672	04/18/2002	Joelle Thonnard	GSKB-120US	1681

26130 7590 12/13/2007

RATNER & PRESTIA- SB DIVISION
ONE WESTLAKES
SUITE 301
BERWYN, PA 19482

EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
12/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/018,672	THONNARD, JOELLE	
	Examiner	Art Unit	
	Padmavathi v. Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *55-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *55, 58, 59, 61- 68* is/are rejected.

7)☒ Claim(s) *56,57 and 60* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/17/07 has been entered.

Status of Claims

2. Claims 55-60, 62 and 64-66 have been amended.

Claims 55-68 are pending and are under examination.

Claim Rejections - 35 USC 112, first paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 55, 58, 59, 61-63, 64-67 and 68 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated recombinant polypeptide comprising the amino acid sequence SEQ ID NO: 2, a fusion protein comprising the amino acid sequence SEQ.ID.NO:2, an immunogenic composition comprising the amino acid sequence SEQ.ID.NO: 2 and a method of inducing an response in a mammal comprising administration of the isolated recombinant polypeptide comprising the amino acid sequence SEQ ID NO: 2 does not reasonably provide enablement for an isolated recombinant polypeptide, fusion protein , immunogenic composition, vaccine and a method of inducing an immune response comprising an immunogenic polypeptide comprising a fragment sequence of at least 15 (the examiner is considering these as variants) contiguous amino acids of SEQ.ID.NO: 2, wherein the isolated polypeptide, when administered to a subject in a composition which can include an adjuvant, or conjugated to a suitable carrier, induces an antibody or T-cell immune response to the polypeptide sequence of SEQ ID NO:2, The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification teaches that Moraxella catarrhalis is a gram negative bacteria and is frequently isolated from upper respiratory tract of humans. It is responsible for several

pathologies , the main one being otitis media in infants and children and pneumoniae in elders. The immune response to this organism is poorly characterized. Strains of M.catarrhalis present variations in their capacity to resist serum bactericidal activity (pages 1-2).

The specification teaches the BASB 111gene , SEQ.ID.NO:1 and the recombinant polypeptide, SEQ.ID.NO:2 from M.catarrhalis strain ATCC 43617 (p. 53and 57). The specification hypothesizes that the claimed polypeptide induces antibodies and would be useful in inhibiting the spread infection . The instant inventors believe that the antigen is likely responsible for the induction bactericidal antibodies when immunized with the polypeptide SEQ.ID.NO:2 and therefore, it could be used in enhancement of lung clearance of M.catarrhalis in mice. The specification states that the administration of peptide fragments is well known for a variety of infection and that one of skill is able to extrapolate the information available for use of peptides to treat diseases associated with M.catarrhalis or antibodies to said peptide fragments (pages 5-6).

One cannot extrapolate the teaching of the specification to the scope of the claims because the claims as written are drawn to variants of SEQ ID NO:2 with undefined alterations of the 276 amino acid residues of SEQ ID NO:2 as well as undefined variants which comprise at least 15 contiguous amino acids of SEQ ID NO:2 and neither the specification nor the art of record define which amino acid residues are critical to the raising of antibodies that are specific for SEQ ID NO:2. As drawn to antibodies, Bowie et al (Science, 1990, 257:1306-1310), teaches that an amino acid sequence encodes a message that determines the shape of a protein and determines the ability of said protein to fold into unique three-dimensional structures that allows them to function. Bowie further teaches that certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (p. 1306, cols 1 and 2). Clearly, the three dimension structure of a protein is critical to the production of antibodies given the teaching of Herbert et al (The Dictionary of Immunology, Academic Press, 3rd Edition, London, 1985, pages 58-59). Herbert et al who specifically teach that an epitope is the region on an antigen molecule to which antibody specifically binds. B cell epitopes on protein antigens are of variable size comprising up to about 20 amino acids. Antibodies bind in a more or less exact three dimensional fit with an epitope. This may be formed from residues on different regions of a protein antigen molecule which, in the native state, are closely apposed due to protein folding. Thus the three-dimensional structure of the protein molecule may be essential for antibody

binding. (p. 58). However, neither the specification nor the art of record provide teachings that provide information about the residues critical for epitopes required for the establishment of an immune response that will produce antibodies that recognize full-length polypeptide, SEQ.ID.NO:2. This information appears to be critical because the art recognizes (see Bowie above) that it is the protein sequence that determines the three dimensional shape of a protein and Herbert et al specifically state that antibodies bind in a more or less exact three dimensional fit and suggests that the three-dimensional structure of the protein molecule may be essential for antibody binding. Thus, in the absence of guidance in the specification, the effects of the undefined alteration of the 169 amino acids of SEQ ID NO:2 on the three-dimensional structure of the claimed isolated protein cannot be predicted and one could not determine how to make the claimed invention or predict that a particularly altered invention would function as claimed with a reasonable expectation of success.

Further, it is noted that a peptide is defined as a compound formed by hydrolytic cleavage of peptides and containing two or more amino acids in Taber's Cyclopedic Medical Dictionary, FA Davis, Philadelphia, 16th Ed., 1985. Given the art recognized definition, the claims drawn to polypeptide peptide comprising an immunogenic fragment of at least 15 contiguous amino acids of SEQ ID NO:2 read on peptides of undefined length and constitution wherein the three dimensional structure of the 15 amino acids comprised within the polypeptides are unknown. Neither the art nor the specification as originally filed provides guidance on how to determine which 15 amino acids will be capable of, when used as an immunogen, raising antibodies which bind specifically to SEQ ID NO:2. In particular, Roitt et al (Immunology, 1993, Mosby, St. Louis, p 7.7-7.8) teach that although it is possible to produce antibodies to almost any part of an antigen, this does not normally happen in an immune response. It is usually found that only a certain areas of the antigen are particularly antigenic, and that a majority of antibodies bind to these regions. These regions are often at exposed areas on the outside of the antigen, particularly where there are loops of polypeptide that lack a rigid tertiary structure (p.7.7-7.8). This is exemplified by the teaching of Holmes (Exp. Opin.Invest. Drugs, 2001, 10(3):511-519) who teaches that rabbits were immunized with synthetic peptides which in each case generated high anti-peptide specific immunoreactivities, however, none of the antibodies exhibited binding to the full length antigen. The author concludes that 'Presumably, expression of these epitopes in the context of the protein was important and affected the antibody binding ability' (p. 513, col 1). Furthermore, the

specification does not take into account the 3 dimensional folding of the native molecule, nor its glycosylation or other post-translational modifications and other characteristics which are of significant importance in an antibody response. Peptides or synthetic antigens cannot effectively substitute for the natural tertiary and quarterary structure of a protein in a physiological situation. Given this teaching, even if the peptides claimed consisted of amino acid residues that were 100% identical to portions of SEQ ID NO:2 it would not be possible to determine with any predictability whether the antibodies produced from a fragment actually bind to SEQ ID NO: 2 in the absence of guidance from the specification.

Further, there is no teaching in the specification of whether or not the epitopes are linear or comprise 3-dimensional structures. In particular, Greenspan et al (Nature Biotechnology, 1999, 7:936-937)teaches that defining epitopes is not as easy as it seems. Even when the epitope is defined, in terms of the spatial organization of residues making contact with ligand, then a structural characterization of the molecular interface for binding is necessary to define the boundaries of the epitope (page 937, 2nd column).

Thus, it would not be expected that the claimed variant proteins, peptides, in the absence of further guidance from the specification, would function as claimed or as contemplated given that there is no teaching of residues critical to the claimed function. Further one would not know how to use the claimed variants that induce a response that does not bind to the full length SEQ ID NO: 2.

The specification provides no guidance or working examples which would provide guidance to one skilled in the art as to which amino acids or polypeptide fragments are critical to the production of antibodies which recognize full length SEQ ID NO:2 and no evidence has been provided which would allow one of skill in the art to predict which of the broadly claimed polypeptide variants would function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

Thus, it would not be expected that the claimed variant proteins in the absence of further guidance from the specification, would function as claimed or as contemplated given that there is no teaching of residues critical to the claimed function. Further the use of said variants that induce response and do not bind to the full length SEQ ID NO:2 . Further one would not know how to use the claimed variants that induce a response but do not bind to the full length SEQ ID NO:2 . The specification provides no guidance or working examples which would provide

guidance to one skilled in the art as to which amino acids are critical for the production of antibodies which recognize an epitope within SEQ ID NO:2 and no evidence has been provided which would allow one of skill in the art to predict which of the broadly claimed polypeptide variants would function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

With respect to vaccine (claims 64-67), enablement of a "vaccine composition" is considered to rest on the teaching of in vivo administration for purposes consistent with the intended use disclosed in the specification. The disclosed intended use for the claimed vaccine is for the treatment of otitis media and respiratory disease caused by Moraxella catarrhalis infections. Thus, the nature of the invention is a therapeutic composition used in the treatment or prevention. In the instant application, the animal to which the claimed composition is administered is merely being used as a bioreactor to make the antibodies (page 59) that may will ultimately be used *in vitro*. In addition, the instant specification does not teach how to use the composition, without undue experimentation, for the prevention or treatment of a disease in the animal to which the substance is administered.

The specification discloses the claimed composition can be used to make antibodies. However, there is insufficient guidance which would enable one skilled in the art to use the claimed compositions for their intended purpose, viz., for the generation of a protective immune response against otitis media and respiratory disease caused by Moraxella catarrhalis infections. At the time the invention was made, vaccines comprising the claimed polypeptide/fragments were not routinely used for the treatment of otitis media and respiratory diseases. The specification lacks guidance by way of general methods or working examples which teach an "effective amount" of the vaccine which would be used for this purpose. Lack of working examples is given added weight in cases involving an unpredictable and undeveloped art, such as immunotherapy of otitis media and respiratory diseases. It is unpredictable whether the claimed composition, which is disclosed as being only immunogenic, would have the added property of generating the protective immune response sufficient to inhibit the otitis media and respiratory diseases because the prior art discloses that vaccine development is at the antigen identification stage and testing of these protective antigens is by testing them in animal models or clinical testing of these antigens (see review article by McMichael, 2000, Microbes and Infection 2; 561-568) The specification has not disclosed a link or nexus between

generating protective immunity using the claimed polypeptide/fragments and preventing or treating *M.catarrhalis* infections or Ottis media. Further, it is not common in the art of immunotherapy to use the claimed compositions for this purpose. Accordingly, there is no objective basis upon which the skilled artisan would reasonably be able to determine or predict an amount of the claimed composition/vaccine effective for its intended use. Therefore, undue experimentation would be required to make and use the invention.

Applicant argues 9/17/07 that Applicant has described a polypeptide antigen having the amino acid sequence of SEQ ID NO:2 and immunogenic fragments. Having adequately described this antigen by sequence, Applicant may properly claim the genus of antibodies that bind to this antigen. This genus of antibodies comprises those that bind to any portion of SEQ ID NO:2, and may accordingly include any antibodies raised from fragments of SEQ ID NO:2.

Applicants' arguments filed on 9/17/07 have been fully considered but they are not deemed to be persuasive because applicant is not claiming an antibody as stated. Further , immunogenicity is not the function of the immunogenic fragment rather it is the property of fragment. In addition the genus of antibodies bind to which portion the SEQ.ID.NO:2 has not been disclosed. Additionally the specification fails to provide which 15 amino acids of SEQ.ID.NO:2 induce an antibody or T-cell response to the full length polypeptide sequence of SEQ.ID.NO:2.

Applicant states that, the specification presents working examples demonstrating that the polypeptide of SEQ ID NO:2 is immunogenic and can generate antibodies that bind to this peptide (Examples 5-7) and screening was necessary to produce an antibody to a particular antigen and was routine in the art of monoclonal antibody production. Screening is routine in the production of all antibodies, not just monoclonal antibodies, because it is important to identify antibodies with the greatest binding affinity. Similarly, screening is routine in the art of vaccine production to identify antigens and antibodies with the greatest vaccine potential. Example 8 describes in detail how to screen antibodies for vaccine potential.

Applicants' arguments filed on 9/17/07 have been fully considered but they are not deemed to be persuasive because it is noted that that although applicant argues that the claimed invention is required to be immunogenic , it is noted for applicant's information that immunogenicity is not considered to be a function of the polypeptide, rather, it is a physical property of the polypeptide. A physical property is a basic or essential attribute shared by all members of class as defined by http://dict.die.net/property. Or a property used to characterize

physical objects as defined by http://wordnet.princeton.edu/perl/webwn. In the instant case, the basic or essential attribute shared by all members of the claimed fragments, the property used to characterize these molecules is that all polypeptides are immunogenic. In point of fact, the only molecule that has a function drawn to the immunogenicity of a polypeptide , is the immune system molecule that binds to it. Thus , as previously set forth, the specification provides no nexus between any structure and function of the broadly claimed fragments. This is especially true given that immunogenicity is not a function of the claimed polypeptide. Although the specification states that the claimed molecules are part of the invention and make reference to a potential method for making it. This does not satisfy the requirements as previously set forth.

Applicant states that, the number or possible fragments having at least contiguous amino acids within amino acids 1-47 and 104-276 of SEQ ID NO:2 is finite, and methods of testing for the immunogenicity of peptides are also merely routine. For example, methods for screening serum for the presence of antibodies are commonly known in the art and commercial kits may be purchased for this purpose.

Applicant's arguments filed on9/17/07 have been fully considered but they are not deemed to be persuasive because the specification discloses an isolated polypeptide comprising the amino acid as set forth in the SEQ.ID.NO:2 and an immunogenic fragment consisting of at least 15 contiguous amino acid of SEQ.ID.NO:2 . However, an having at least contiguous amino acids within amino acids 1-47 and 104-276 of SEQ ID NO:2 are not enabled for the reasons as discussed above in the written description Para# 3. Although applicant argues that it is routine in the art to generate fragments and to determine whether or not those fragments are immunogenic and bind to an antibody , the requirement of 35 USC 112 first paragraph are drawn to teaching of how to make and use the claimed invention and are not drawn to screening of molecules in order to determine whether or not the invention would function as claimed. However, the screening assays suggested by applicant do not enable the claimed invention because the court found in Rochester v. Searle, 358 F.3d 916, Fed Cir., 2004 that screening assays are not sufficient to enable an invention since they are merely a wish or plan for obtaining the claimed chemical invention. It is clear that the Applicant's argument that the specification does provide the necessary guidance to the practitioner to enable the making of the broadly claimed invention, that is the ability to predictably distinguish between those molecules that are immunogenic from those that are not . Since the making of the broadly claimed invention is not enabled, one would not know how to use the broadly claimed invention.

Therefore, it is appropriate to maintain the rejection.

Claim Rejections - 35 USC 112, first paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 55, 58,59, 61, 62, 63-64, 66, 67 and 68 are rejected under 35 USC 112, first paragraph , as the specification does not contain a written description of the claimed invention (This is a new matter rejection).

The limitation "an immunogenic polypeptide comprising a fragment sequence of at least 15 amino acids having an aligned contiguous segment from amino acid positions 1- 47 or amino acid positions 104-276 of SEQ ID NO:2" claimed in claims 55, 58,59, 61, 62, 63-64, 66, 67 and 68 has no clear support in the specification and the claims as originally filed.
Applicant pointed to support for the immunogenic polypeptide comprising a fragment sequence of at least 15 amino acids having an aligned contiguous segment from amino acid positions 1-47 or amino acid positions 104-276 of SEQ ID NO:2" in original claim 28 filed by preliminary amendment with the national application , and in the listing of SEQ.ID.NO:2. A review of the specification discloses support for immunogenic polypeptide comprising a fragment sequence of at least 15 amino acids having an aligned contiguous segment from amino acid positions 1-47 or amino acid positions 104-276 of SEQ ID NO:2". The suggested support is not found persuasive because there is nothing in the specification to suggest the specific polypeptide comprising a fragment sequence of at least 15 amino acids having an aligned contiguous segment from amino acid positions 1-47 or amino acid positions 104-276 of SEQ ID NO:2. Further, there is no mention of specific amino acid positions 1-47 or amino acid positions 104-276 of SEQ ID NO:2. The subject matter claimed in claims 55, 58,59, 61, 62, 63-64, 66, 67 and 68 broadens the scope of the invention as originally disclosed in the specification.

Claim Rejections - 35 USC 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21 (2) of such treaty in the English language.

The transitional limitation "comprises" similar to the limitations, such as, "has", "includes," "contains," or "characterized by," represents open-ended claim language and therefore does not exclude additional, unrecited elements. See M.P.E.P 2111.03 [R-I]. See Molecular Research Corp. v. CBS, Inc., 793 F2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open. for the inclusion of unspecified ingredients even in major amounts". On the other hand, the limitation "consisting of represents closed claim language and excludes any element, step, or ingredient not specified in the claim. In re Gray, 53 F. 2d 520, II USPQ 255 (CCPA 1931); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948).

8. Claims 55, 58, 59, 61-64 and 66- 68 are rejected under 35 U.S.C. 102(e) as being anticipated by Breton U.S.Patent 6605709.

Breton as shown below discloses an isolated polypeptide comprising an amino acid sequence SEQ.ID.NO:6534 comprising an immunogenic fragment which has 15 contiguous amino acids and is 100% identical with the claimed polypeptide (please see the sequence alignment, QY indicates SEQ.ID.NO: 2 of the claimed invention and Db represents the prior art protein) and thus anticipated claims 55, 58. The prior art discloses maltose receptor (outer membrane protein of E.coli) as a peptide fusion partner (column 34, lines 15-30 in patent) and thus discloses fusion protein as claimed in claim 59. Further the prior art discloses a vaccine composition (intended use of composition) comprising M.catarrhalis polypeptide, SEQ.ID.NO: 6534 with pharmaceutical carrier such as buffer, adjuvant, glycerol etc (see column 37-38) or killed E.coli preparation with an immunogenic fragment of peptide of the invention expressed on its surface or E.coli lysate, wherein the killed E.coli acts a carrier (see column 39, lines 58-63). Further, the prior art discloses one or more surface proteins as vaccine a composition (see column 37, lines 8-20) for M.catarrahalis and thus anticipates a vaccine composition comprising immunogenic fragments /polypeptide and one other M.catarrhalis antigen in a pharmaceutical carrier as claimed in claims 62, 63, 64 and 66. The prior art also anticipated claim 68, a method for inducing an antibody response as mice or rabbit or hamsters can be immunized (administered) with immunogenic fragment such as the disclosed polypeptide, SEQ.ID.NO: 6534 (see column 40, lines 16-21). Therefore, the claimed invention is anticipated by the prior art.

US-09-543-681A-6534
; Sequence 6534, Application US/09543681A

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; Patent No. 6605709
; GENERAL INFORMATION:
;  APPLICANT: GARY BRETON
;  TITLE OF INVENTION: NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO PROTEUS MIRABILIS FOR
;  TITLE OF INVENTION:  DIAGNOSTICS AND THERAPEUTICS
;  FILE REFERENCE: 2709.1002-001
;  CURRENT APPLICATION NUMBER: US/09/543,681A
;  CURRENT FILING DATE:  2000-04-05
;  PRIOR APPLICATION NUMBER: US 60/128,706
;  PRIOR FILING DATE: 1999-04-09
;  NUMBER OF SEQ ID NOS: 8344
; SEQ ID NO 6534
;   LENGTH: 279
;   TYPE: PRT
;   ORGANISM: Proteus mirabilis
US-09-543-681A-6534

  Query Match             5.8%;  Score 16;  DB 4;  Length 279;
  Best Local Similarity   100.0%;  Pred. No. 2e-07;
  Matches   16;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        224 FVEDKDSPYVNIIVAR 239
              ||||||||||||||||
Db        227 FVEDKDSPYVNIIVAR 242
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9. Claims 55, 58 and 62 under 35 U.S.C. 102(b) as being anticipated by Murphy et al 1993 Gene 129, 107-111, 1993 Or Fleischmann et al Science 269, 496-512, 1995

Murphy et al as show below disclose an isolated polypeptide comprising an immunogenic polypeptide comprising a fragment of at least 15 amino acids that matches 100% with an aligned contiguous segment of SEQ.ID.NO: 2 (please see the sequence alignment, from position 140-173, QY represents SEQ.ID.NO: 2 of the claimed invention and Db represents the prior art protein) and thus anticipated claims 55, 58 and 62. The prior art polypeptide reads on claims because the disclosed immunogenic fragment comprises more than 15 amino acids and is common in the art of immunology to use a peptide with five amino acids to induce an antibody response in animals, therefore, the disclosed polypeptide comprising 276 amino acids is inherently immunogenic and thus comprises an immunogenic fragments as claimed in claims. Therefore, the claimed invention is anticipated by the prior art.

```
R;Murphy, G.L.; Whitworth, L.C.
Gene 129, 107-111, 1993
A;Title: Analysis of tandem, multiple genes encoding 30-kDa membrane proteins in Pasteurella
haemolytica A1.
A;Reference number: JN0751; MUID:93328110; PMID:8335249
A;Accession: JN0751
A;Molecule type: DNA
A;Residues: 1-277
A;Cross-references: GB:L11037; NID:g349529; PIDN:AAA25538.1; PID:g349530
A;Experimental source: serotype A1
A;Note: this protein displays a high degree of identity with an Escherichia coli inner membrane
lipoprotein and an haemophilus influenzae membrane protein
C;Comment: This protein is important in eliciting immunity to pneumonic pasteurellosis.
C;Superfamily: lipoprotein-28
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C;Keywords: membrane protein

  Query Match             12.3%;  Score 34;  DB 2;  Length 277;
  Best Local Similarity   100.0%;  Pred. No. 8e-26;
  Matches   34;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        140 IAVPNDPSNLARALILLEKQGLIKLKDNTNLFST 173
              |||||||||||||||||||||||||||||||||
Db        141 IAVPNDPSNLARALILLEKQGLIKLKDNTNLFST 174
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Or

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R;Fleischmann, R.D.; Adams, M.D.; White, O.; Clayton, R.A.; Kirkness, E.F.; Kerlavage, A.R.;
Bult, C.J.; Tomb, J.F.; Dougherty, B.A.; Merrick, J.M.; McKenney, K.; Sutton, G.; FitzHugh, W.;
Fields, C.; Gocayne, J.D.; Scott, J.; Shirley, R.; Liu, L.I.; Glodek, A.; Kelley, J.M.; Weidman,
J.F.; Phillips, C.A.; Spriggs, T.; Hedblom, E.; Cotton, M.D.; Utterback, T.R.; Hanna, M.C.;
Nguyen, D.T.; Saudek, D.M.; Brandon, R.C.; Fine, L.D.; Fritchman, J.L.; Fuhrmann, J.L.;
Geoghagen, N.S.M.
Science 269, 496-512, 1995
A;Authors: Gnehm, C.L.; McDonald, L.A.; Small, K.V.; Fraser, C.M.; Smith, H.O.; Venter, J.C.
A;Title: Whole-genome random sequencing and assembly of Haemophilus influenzae Rd.
A;Reference number: A64000; MUID:95350630; PMID:7542800
A;Accession: B64082
A;Status: nucleic acid sequence not shown; translation not shown
A;Molecule type: DNA
A;Residues: 1-273
A;Cross-references: GB:U32744; GB:L42023; NID:g1573608; PIDN:AAC22279.1; PID:g1573614;
TIGR:HI0620
A;Experimental source: strain Rd KW20
R;Chanyangam, M.; Smith, A.L.; Moseley, S.L.; Kuehn, M.; Jenny, P.
Infect. Immun. 59, 600-608, 1991
A;Title: Contribution of a 28-kilodalton membrane protein to the virulence of Haemophilus
influenzae.
A;Reference number: A43581; MUID:91100034; PMID:1987077
A;Accession: A43581
A;Status: preliminary
A;Molecule type: DNA
A;Residues: 21-248,'V',250-273
A;Cross-references: GB:M59804
C;Superfamily: lipoprotein-28
C;Keywords: membrane protein

  Query Match              6.9%;  Score 19;  DB 2;  Length 273;
  Best Local Similarity   100.0%;  Pred. No. 7.6e-11;
  Matches   19;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        107 LNNLVIVGNTFVYPLAGYS 125
              |||||||||||||||||||
Db        104 LNNLVIVGNTFVYPLAGYS 122
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Remarks

10. No claims are allowed.

Conclusion

11. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Right Fax number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week. If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Shanon Foley can be reached on (571) 272-0898. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

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